UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,164	09/09/2003	Randal Lee Schapaugh	00373.US1	5673

25533 7590 03/06/2007

PHARMACIA & UPJOHN
7000 Portage Road
KZO-300-104
KALAMAZOO, MI 49001

EXAMINER	
WALLENHORST, MAUREEN	
ART UNIT	PAPER NUMBER
1743	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,164	SCHAPAUGH ET AL.	
	Examiner	Art Unit	
	Maureen M. Wallenhorst	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-11,13-17,19-24,27,29-32,35 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-11,13-17,19-24,27,29-32,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/3/04,4/15/04, 6/25/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. Claims 1-2, 5-11, 13-17, 19-24, 27, 29-32 and35-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

On lines 15-16 of claim 1, the phrase "the sample taken from the aqueous dissolution medium" lacks antecedent basis.

In claim 6, the phrase "the pharmaceutically active component" lacks antecedent basis.

On line 1 of claim 23, the phrase "the stirring" lacks antecedent basis since neither claim 1 nor claim 22 positively recites any step of stirring.

On line 1 of claim 27, the phrase "the buffer solution" should be changed to –the buffer—since claim 1 only positively recites a buffer, not a buffer solution.

In claim 29, the phrase "the phosphate buffer at pH ranging from 6 to 7" lacks antecedent basis since claim 29 depends from claim 27, and claim 27 only positively recites a phosphate buffer having a pH ranging from 6 to 8, not 6 to 7.

On lines 19-20 of claim 35, the phrase "the sample taken from the aqueous dissolution medium" lacks antecedent basis. On line 20 of claim 35, the word "befor" is misspelled.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-2, 5-11, 13-17, 19, 21-24, 27, 29-30 and 35 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 5-26, 28 and 33-36 of copending Application No. 10/658,165 in view of Andonaegui et al (article submitted in the Information Disclosure Statement filed on March 3, 2004). Claims 1-3, 5-26, 28 and 33-36 of U.S. Application serial no. 10/658,165 recite a method of characterizing the transfer of an analyte from a non-aqueous liquid composition to an aqueous dissolution medium comprising the steps of providing a non-aqueous liquid composition comprising an analyte and a non-aqueous base, combining the non-aqueous liquid composition with an aqueous dissolution medium, agitating and mixing the non-aqueous liquid composition and the aqueous dissolution medium and determining the amount of analyte in the aqueous dissolution medium at multiple time points after the combining and agitating steps. The claims of U.S. application

serial no. 10/658,165 fail to recite that a non-aqueous diluent is added to the non-aqueous liquid composition prior to being mixed with the aqueous dissolution medium.

Andonaegui et al teach of an in vitro test for studying the in vivo performance of sustained release tablets containing theophylline therein as administered under a fasting condition and with a high fat diet. Andonaegui et al teach that tablets having a non-aqueous lipid matrix and theophylline therein are combined with an aqueous dissolution medium such as water, simulated gastric fluid, and aqueous mediums with gradual pH changes in a dissolution apparatus such as a paddle assembly. Theophylline dissolved into the aqueous dissolution medium after a predetermined time is analyzed by UV spectrophotometry. Andonaegui et al teach that in order to simulate the in vivo action of the theophylline drug under the condition of a high fat diet, the tablet is pretreated or diluted with peanut oil before being combined with the aqueous dissolution medium. Changes produced in the in vivo absorption profile of the drug by a high fat diet are correlated better with a pretreatment of the tablets with peanut oil followed by a dissolution test using an aqueous medium. See pages 1199-1200 and 1203 of Andonaegui et al.

Based upon the combination of claims 1-3, 5-26, 28 and 33-36 in U.S. application serial no. 10/658,165 and Andonaegui et al., it would have been obvious to one of ordinary skill in the art at the time of the instant invention to dilute the non-aqueous liquid composition recited in the claims of U.S. application serial no. 10/658,165 with a non-aqueous diluent before combining the non-aqueous liquid composition with an aqueous dissolution medium for dissolution testing in order to simulate an in vivo condition of the analyte in the non-aqueous liquid composition under a high fat diet, as taught by Andonaegui et al.

This is a provisional obviousness-type double patenting rejection.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 1-2, 5-11, 13-17, 19, 21-24, 27, 29-31 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schapaugh et al (US 2004/0115822) in view of Andonaegui et al (article submitted in the Information Disclosure Statement filed on March 3, 2004). For a teaching of Andonaegui et al, see previous paragraphs in this Office action.

Schapaugh et al teach of a method for measuring the dissolution rate of an analyte in a non-aqueous liquid composition. The method comprises the steps of providing a non-aqueous liquid composition comprising an analyte and a non-aqueous base, combining the non-aqueous liquid composition with an aqueous dissolution medium, agitating the non-aqueous liquid composition and the aqueous dissolution medium, and determining the amount of analyte in the aqueous dissolution medium at different points in time. Schapaugh et al also teach that the aqueous dissolution medium can be filtered through a filter before determining the amount of

analyte therein. Preferably, the non-aqueous liquid composition is a sustained release pharmaceutical composition having ceftiofur as the analyte therein and oil such as cottonseed oil as the aqueous base. The non-aqueous liquid composition is a suspension, solution or emulsion, and the agitation is conducted until from about 10%-100% of the total amount of analyte has been dissolved in the aqueous dissolution medium. The aqueous dissolution medium can contain a buffer such as a phosphate buffer having a molarity from 0.001 molar (1mM) to 0.1 molar (100 mM) and a pH of 6 to 8. The ratio of the non-aqueous liquid composition to the aqueous dissolution medium varies from about 1:100 to about 1:2000 by volume. See paragraph nos. 0037-0038 and 0046, and the claims in Schapaugh et al. The reference to Schapaugh et al qualifies as prior art against the instant claims under 35 USC 102(e) since the effective filing date of this reference (September 12, 2002) is prior to the effective filing date of the instant application (November 27, 2002), and the reference to Schapaugh et al has a different inventive entity than the instant application. Schapaugh et al fail to teach that a non-aqueous diluent is added to the non-aqueous liquid composition prior to being mixed with the aqueous dissolution medium.

Based upon the combination of Schapaugh et al and Andonaegui et al., it would have been obvious to one of ordinary skill in the art at the time of the instant invention to dilute the non-aqueous liquid composition taught by Schapaugh et al with a non-aqueous diluent before combining the non-aqueous liquid composition with an aqueous dissolution medium for dissolution testing in order to simulate an in vivo condition of the analyte in the non-aqueous liquid composition under a high fat diet, as taught by Andonaegui et al.

8. Claims 1-2, 5-11, 13-17, 19, 21-24, 27, 29-32 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dunn et al (US Patent no. 5,721,359, submitted in the IDS filed on March 3, 2004) in view of both Andonaegui et al (article submitted in the IDS filed on March 3, 2004) and Conti et al (article submitted in the IDS filed on March 3, 2004). For a teaching of Andonaegui et al, see previous paragraphs in this Office action.

Dunn et al teach of a non-aqueous liquid composition containing a non-aqueous base and an analyte. The non-aqueous base is oil such as corn oil, peanut oil, sesame oil, olive oil, safflower oil, soybean oil, cottonseed oil, rapeseed oil and mixtures thereof. Preferably, the non-aqueous base is cottonseed oil. The analyte is a cephalosporin antibiotic material known as ceftiofur. The non-aqueous liquid composition is used as a pharmaceutical composition in a sustained release dosage form. The pharmaceutical composition can also contain excipients such as dispersing agents, emulsifying agents, buffers, sweeteners, flavoring agents, colorants and preservative agents. See lines 10-39 in column 3 and lines 21-31 in column 9 of Dunn et al. In example 4 of Dunn et al, a sustained release oil formulation containing ceftiofur free acid and cottonseed oil is taught. In example 7 of Dunn et al, an in vitro dissolution test of the ceftiofur oil suspension formulation is disclosed in order to characterize the in vivo performance of this pharmaceutical composition for public use. In the dissolution test, samples of the non-aqueous liquid oil composition containing ceftiofur antibiotic are loaded into a dissolution apparatus containing an aqueous dissolution medium at an optimal pH of 7. The non-aqueous liquid composition and the aqueous dissolution medium are agitated with a rotating paddle, and at different time points after being combined together, samples of the aqueous dissolution medium are taken and tested for the amount of ceftiofur analyte therein. See Figure 6 in Dunn et al that

plots the amount of ceftiofur analyte released into the aqueous dissolution medium as a function of time. Dunn et al fail to teach that a non-aqueous diluent is added to the non-aqueous liquid composition prior to being mixed with the aqueous dissolution medium, and fail to teach that the aqueous dissolution medium contains a buffer of a certain molarity.

Conti et al teach of in vitro dissolution tests for different drug delivery systems. Four different types of dissolution methods and apparatuses are evaluated including a paddle stirring apparatus, a rotating bottle apparatus, a shaker incubator and a recycling flow through cell. In each of these devices, the aqueous dissolution medium used is an aqueous phosphate buffered solution at an optimal pH of 7.4. In some of the tests performed, the surfactant Polysorbate 20 is added to the aqueous dissolution medium. In each of the dissolution tests, samples of the aqueous dissolution medium are taken at different time points after being admixed with a drug formulation, then are filtered through a Millipore membrane having 0.22 micron pores, and analyzed by UV spectrophotometry. See pages 1224-1226 in Conti et al. Conti et al teach that the presence of a surfactant in the aqueous dissolution medium doubles the amount of drug released into the dissolution medium for all of the methods tested. Faster drug release is also found for the aqueous dissolution medium containing a phosphate buffer at pH 7.4 and at a high ionic strength.

Based upon the combination of Dunn et al and Andonaegui et al., it would have been obvious to one of ordinary skill in the art at the time of the instant invention to dilute the non-aqueous liquid composition taught by Dunn et al with a non-aqueous diluent before combining the non-aqueous liquid composition with an aqueous dissolution medium for dissolution testing

in order to simulate an in vivo condition of the analyte in the non-aqueous liquid composition under a high fat diet, as taught by Andonaegui et al.

Based upon the combination of Dunn et al and Conti et al, it would have been obvious to one of ordinary skill in the art to use a phosphate buffered aqueous solution as the aqueous dissolution medium in the dissolution method taught by Dunn et al since Conti et al disclose that such a phosphate buffered dissolution medium serves to produce faster drug release from a drug formulation into the aqueous medium, and that a phosphate buffer at a high ionic strength, which is determined by the molarity of the phosphate buffer, produces an even faster drug release into an aqueous dissolution medium. Since concentration is a result effective variable, one of ordinary skill in the art at the time of the instant invention would have found it obvious to vary the molarity of the phosphate buffer used as an aqueous dissolution medium in a dissolution test to the values recited in instant claim 1 in order to optimize the action of the aqueous dissolution medium for dissolving a drug for analysis. With regards to instant claims 30-31, it would have been obvious to one of ordinary skill in the art to vary the ratio of the non-aqueous liquid composition to the aqueous dissolution medium taught by Dunn et al to the levels recited since the amount of materials used in a method is a result effective variable that can be experimentally varied in order to optimize a particular procedure being performed with the materials.

9. Claims 20 and 36 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims since none of the prior art of record teaches or fairly suggests diluting a non-aqueous liquid composition comprising an analyte/drug with a

hydrogenated coconut oil or a modified cottonseed oil prior to testing the non-aqueous liquid composition in a dissolution testing apparatus containing an aqueous dissolution medium.

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Please make note of: Qureshi, Hutchins et al, Muller, Fassihi, Benz, Smolen, Goodhart et al and Kirschner et al who all teach of devices for performing dissolution tests on pharmaceutical compositions.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maureen M. Wallenhorst whose telephone number is 571-272-1266. The examiner can normally be reached on Monday-Thursday from 6:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden, can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maureen M. Wallenhorst
Primary Examiner
Art Unit 1743

mmw

March 1, 2007

Maureen M. Wallenhorst
MAUREEN M. WALLENHORST
PRIMARY EXAMINER
GROUP [redacted] 1700